

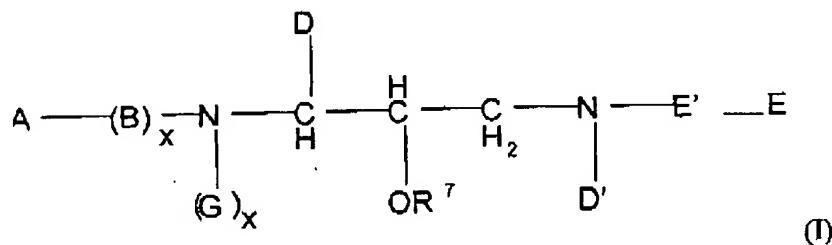
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Amendments to the Claims

NOV 27 2006

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently amended) A compound of formula I:



or a pharmaceutically acceptable salt thereof, wherein:

E' is $\text{[-CO- or] } -\text{SO}_2^-$;

A is selected from $-\text{R}^1\text{-C}_1\text{-C}_6$ alkyl, which is optionally substituted with one or more groups independently selected from hydroxy, $\text{C}_1\text{-C}_4$ alkoxy, Ht, $-\text{O-Ht}$, $-\text{NR}^2\text{-CO-N(R}^2\text{)}_2$, $-\text{SO}_2\text{-R}^2$ or $-\text{CO-N(R}^2\text{)}_2$; or $-\text{R}^1\text{-C}_2\text{-C}_6$ alkenyl, which is optionally substituted with one or more groups independently selected from hydroxy, $\text{C}_1\text{-C}_4$ alkoxy, Ht, $-\text{O-Ht}$, $-\text{NR}^2\text{-CO-N(R}^2\text{)}_2$ or $-\text{CO-N(R}^2\text{)}_2$; or R^7 ;

R^1 is $-\text{O-C(O)-}$;

each Ht is independently selected from $\text{C}_3\text{-C}_7$ cycloalkyl; $\text{C}_5\text{-C}_7$ cycloalkenyl; $\text{C}_6\text{-C}_{14}$ aryl; or a 5-7 membered saturated or unsaturated heterocycle, containing one or more heteroatoms selected from N, O, or S; wherein said aryl or said heterocycle is optionally fused to Q; and wherein any member of said Ht is optionally substituted with one or more substituents independently selected from oxo, $-\text{OR}^2$, SR^2 , $-\text{R}^2$, $-\text{N(R}^2\text{)(R}^2\text{)}$, $-\text{R}^2\text{-OH}$, $-\text{CN}$, $-\text{CO}_2\text{R}^2$, $-\text{C(O)-N(R}^2\text{)}_2$, $-\text{S(O)}_2\text{-N(R}^2\text{)}_2$, $-\text{N(R}^2\text{)-C(O)-R}^2$, $-\text{N(R}^2\text{)-C(O)O-R}^2$, $-\text{C(O)-R}^2$, $-\text{S(O)}_n\text{-R}^2$, $-\text{OCF}_3$, $-\text{S(O)}_n\text{-Q}$, methylenedioxy, $-\text{N(R}^2\text{)-S(O)}_2\text{(R}^2\text{)}$, halo, $-\text{CF}_3$, $-\text{NO}_2$, Q, $-\text{OQ}$, $-\text{OR}^7$, $-\text{SR}^7$, $-\text{R}^7$, $-\text{N(R}^2\text{)(R}^7\text{)}$ or $-\text{N(R}^7\text{)}_2$;

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each Q is independently selected from a 3-7 membered saturated, partially saturated or unsaturated carbocyclic ring system; or a 5-7 membered saturated, partially saturated or unsaturated heterocyclic ring containing one or more heteroatoms selected from O, N, or S; wherein Q is optionally substituted with one or more groups selected from oxo, -OR², -R², -SO₂R², -SO₂-N(R²)₂, -N(R²)₂, -N(R²)-C(O)-R², -R²-OII, -CN, -CO₂R², -C(O)-N(R²)₂, halo, -ClF₃;

each R² is independently selected from H, or C₁-C₄ alkyl; and wherein said alkyl, when not a substituent of Q, is optionally substituted with Q or -OR³; wherein when said R² is an -OR³ substituted moiety, said R³ in -OR³ may not be -OR² substituted;

B is absent, when present, is -N(R²)-C(R³)₂-C(O)-;

each x is independently 0 or 1;

each R³ is independently selected from H, Ht, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl or C₅-C₆ cycloalkenyl; wherein any member of said R³, except H, is optionally substituted with one or more substituents selected from -OR², -C(O)-NH-R², -S(O)_n-N(R²)(R²), -N(R²)₂, -N(R²)-C(O)-O(R²), -N(R²)-C(O)-N(R²), -N(R²)-C(O)-(R²), Ht, -CN, -SR², -CO₂R², or NR²-C(O)-R²;

each n is independently 1 or 2;

G is H, when present, is selected from H, R⁷ or C₁-C₄ alkyl, or, when G is C₁-C₄ alkyl, G and R⁷ are optionally bound to one another either directly or through a C₁-C₃ linker to form a heterocyclic ring; or

when G is not present, the nitrogen to which G is attached is bound directly to the R⁷ group in -OR⁷ with the concomitant displacement of one ZM group from R⁷;

D is selected from Q; C₁-C₆ alkyl optionally substituted with one or more groups selected from C₃-C₆ cycloalkyl, -OR², -S-Ht, -R³, -O-Q or Q; C₂-C₆ alkenyl optionally substituted with one or more groups selected from -OR², -S-Ht, -R³, -O-Q or Q; C₃-C₆

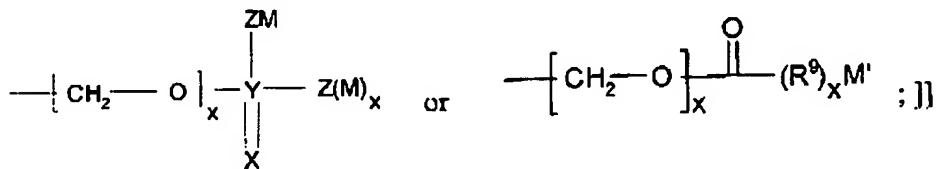
~~cycloalkyl optionally substituted with or fused to Q; or C₅-C₆-cycloalkenyl optionally substituted with or fused to Q;~~

D' is selected from C₁-C₁₅ alkyl, C₂-C₁₅ alkenyl or C₂-C₁₅ alkynyl, each of which contains one or more substituents selected from oxo, [[halo,]] -CF₃, -OCF₃, -NO₂, azido, -SH, -[SR³], -N(R³)-N(R³)₂, -O-N(R³)₂, -(R³)N-O-(R³), [[-N(R³)₂,]] -CN, -CO₂R³, -C(O)-N(R³)₂, -S(O)_n-N(R³)₂, -N(R³)-C(O)-R³, -N(R³)-C(O)-N(R³)₂, -N(R³)-C(O)-S(R³), -C(O)-R³, [[-S(O)_n-R³,]] -N(R³)-S(O)_n(R³), -N(R³)-S(O)_n-N(R³)₂, -S-NR³-C(O)R³, -C(S)N(R³)₂, -C(S)R³, -NR³-C(O)OR³, -O-C(O)OR³, -O-C(O)N(R³)₂, -NR³-C(S)R³, =N-OH, =N-OR³, =N-N(R³)₂, =NR³, -NNR³C(O)N(R³)₂, =NNR³C(O)OR³, =NNR³S(O)_n-N(R³)₂, -NR³-C(S)OR³, -NR³-C(S)N(R³)₂, -NR³-C[=N(R³)]-N(R³)₂, -N(R³)-C[=N-NO₂]-N(R³)₂, -N(R³)-C[=N-NO₂]-OR³, -N(R³)-C[=N-CN]-OR³, -N(R³)-C[=N-CN]-(R³)₂, -OC(O)R³, -OC(S)R³, -OC(O)N(R³)₂, -C(O)N(R³)-N(R³)₂, -O-C(O)N(R³)-N(R³)₂, O-C(O)N(OR³)(R³), N(R³)-N(R³)C(O)R³, N(R³)-OC(O)R³, N(R³)-OC(O)R³, N(R³)-OC(S)N(R³)₂, -OC(S)N(R³)(R³), or PO₃-R³; with the proviso that when R⁷ is H, E' is SO₂, G is H or alkyl, and when B is present or when B is not present and R⁴ is C(O), D' may not be C₁-C₁₅ alkyl substituted with one substituent selected from N(R³)₂, -SR³ or S(O)_n-R³, or substituted with two N(R³)₂ substituents;

E is selected from Ht; O-Ht; Ht-IIIt; Ht fused with Ht; -O-R³; -N(R²)(R³); C₁-C₆ alkyl optionally substituted with one or more groups selected from R⁴ or Ht; C₂-C₆ alkenyl optionally substituted with one or more groups selected from R⁴ or Ht; C₃-C₆ saturated carbocycle optionally substituted with one or more groups selected from R⁴ or Ht; or C₅-C₆ unsaturated carbocycle optionally substituted with one or more groups selected from R⁴ or Ht;

each R⁴ is independently selected from -OR², -OR³, -SR², -SOR², -SO₂R², -CO₂R², -C(O)-NHR², -C(O)-N(R²)₂, -C(O)-NR²(OR²), -S(O)₂-NHR², halo, -NR²-C(O)-R², -N(R²)₂ or -CN; and

each R⁷ is independently selected from hydrogen, H,



~~wherein each M is independently selected from H, Li, Na, K, Mg, Ca, Ba, N(R³)₄, C₁-C₄-alkyl, C₂-C₁₂-alkenyl, or R⁶; wherein 1 to 4 CH₂ radicals of the alkyl or alkenyl group, other than the CH₂ that is bound to Z, is optionally replaced by a heteroatom group selected from O, S(O), S(O)₂, or N(R³); and wherein any hydrogen in said alkyl, alkenyl or R⁶ is optionally replaced with a substituent selected from -O-, OR², R², N(R³)₂, N(R³)₃, R²OH, CN, CO₂R², C(O)N(R³)₂, S(O)₂N(R³)₂, N(R³)C(O)R³, C(O)R², S(O)_nR², OCF₃, S(O)_nR⁶, N(R³)S(O)₂(R²), S(O)₂(R²), halo, -CF₃, or -NO₂;~~

~~M' is H, C₁-C₄-alkyl, C₂-C₁₂-alkenyl, or R⁶; wherein 1 to 4 CH₂ radicals of the alkyl or alkenyl group is optionally replaced by a heteroatom group selected from O, S, S(O), S(O)₂, or N(R³); and wherein any hydrogen in said alkyl, alkenyl or R⁶ is optionally replaced with a substituent selected from -O-, OR², R², N(R³)₂, N(R³)₃, R²OH, CN, CO₂R², C(O)N(R³)₂, S(O)₂N(R³)₂, N(R³)C(O)R₂, C(O)R², S(O)_nR², OCF₃, S(O)_nR⁶, N(R³)S(O)₂(R²), halo, -CF₃, or -NO₂;~~

~~Z is O, S, N(R³)₂, or, when M is not present, H.~~

~~V is P or S;~~

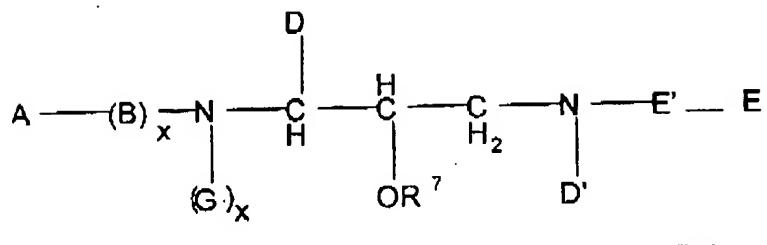
~~X is O or S;~~

~~R⁹ is C(R³)₂, O or N(R²); and wherein when V is S, Z is not S;~~

~~R⁶ is a 3-6 membered saturated, partially saturated or unsaturated carbacyclic or heterocyclic ring system, or an 8-10 membered saturated, partially saturated or unsaturated bicyclic ring system; wherein any of said heterocyclic ring systems contains one or more heteroatoms selected from O, N, S, S(O)_n or N(R³); and wherein any of said ring systems optionally contains 1 to 4 substituents independently selected from OH, C₁-C₄-alkyl, O-C₁-C₄-alkyl or O-C(O)-C₁-C₄-alkyl; and~~

~~each R⁵ is independently selected from hydrogen, C₁-C₄-alkyl, C₂-C₈-alkenyl, C₂-C₈-alkynyl or Ht, wherein any R⁵, except for hydrogen, is optionally substituted with -CF₃, -PO₃R³, azido or halo.~~

2. (Currently amended) The compound according to claim 1, having the formula IA:



wherein:

D' is selected from C₁₋₁₅ alkyl, C₂₋₁₅ alkenyl or C_{2-C₁₅} alkynyl; each of which is substituted with one to two -CN groups and each of which is optionally substituted with C_{3-C₈} cycloalkyl.

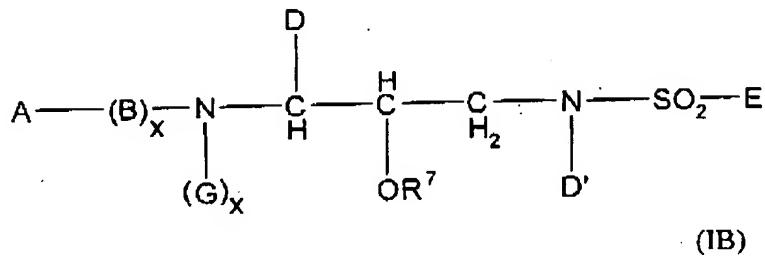
3. (Currently amended) The compound according to claim 2 wherein:

D' is selected from C₁₋₁₅ alkyl or C₂₋₁₅ alkenyl; each of which is substituted with one to two -CN groups and each of which is optionally substituted with C_{3-C₈} cycloalkyl.

4. (Currently amended) The compound according to claim 2 wherein:

D' is C_{2-C₁₅} alkynyl which is substituted with one to two -CN groups and each of which is optionally substituted with C_{3-C₈} cycloalkyl.

5. (Currently amended) The compound according to claim 1 having the formula IIB:



wherein:

D' is selected from C₁-C₁₅ alkyl, C₂-C₁₅ alkenyl or C₂-C₁₅ alkynyl, each of which contains one or more substituents selected from oxo, [[halo,]]-CF₃, -OCF₃, -NO₂, azido, -SH, [[-SR³,]]-N(R³)-N(R³)₂, -O-N(R³)₂, -(R³)N-O-(R³), [[-N(R³)₂,]]-CO₂R³, -C(O)-N(R³)₂, -S(O)_n-N(R³)₂, -N(R³)-C(O)-R³, -N(R³)-C(O)-N(R³)₂, -N(R³)-C(O)-S(R³), -C(O)-R³, [[-S(O)_n-R³,]]-N(R³)-S(O)_n(R³), -N(R³)-S(O)_n-N(R³)₂, -S-NR³-C(O)R³, -C(S)N(R³)₂, -C(S)R³, -NR³-C(O)OR³, -O-C(O)OR³, -O-C(O)N(R³)₂, -NR³-C(S)R³, =N-OII, =N-OR³, =N-N(R³)₂, =NR³, =NNR³C(O)N(R³)₂, =NNR³C(O)OR³, =NNR³S(O)_n-N(R³)₂, -NR³-C(S)OR³, -NR³-C(S)N(R³)₂, -NR³-C[=N(R³)]-N(R³)₂, -N(R³)-C[=N-NO₂]-N(R³)₂, -N(R³)-C[=N-NO₂]-OR³, -N(R³)-C[=N-CN]-OR³, -N(R³)-C[=N-CN]-R³, -OC(O)R³, -OC(S)R³, -OC(O)N(R³)₂, -C(O)N(R³)-N(R³)₂, -O-C(O)N(R³)-N(R³)₂, O-C(O)N(OR³)(R³), N(R³)-N(R³)C(O)R³, N(R³)-OC(O)R³, N(R³)-OC(O)R³, N(R³)-OC(S)N(R³)₂, -OC(S)N(R³)(R³), or PO₃-R³; with the proviso that when R³ is H, E' is SO₂, G is H or alkyl, and when B is present or when B is not present and R¹ is C(O), D' may not be C₁-C₁₅ alkyl substituted with one substituent selected from -N(R³)₂, -SR³ or -S(O)_n-R³, or substituted with two -N(R³)₂ substituents.

6. (Currently amended) The compound according to claim 5 wherein:

D' is selected from C₁-C₁₅ alkyl or C₂-C₁₅ alkenyl, each of which contains one or more substituents selected from oxo, [[halo,]] -CF₃, -OCF₃, -NO₂, azido, -N(R³)-N(R³)₂, -O-N(R³)₂, -(R³)N-O-(R³), [[-N(R³)₂,]] -N(R³)-C(O)-N(R³)₂, -N(R³)-C(O)-S(R³), -C(O)-R³, [[-S(O)_n-R³,]]

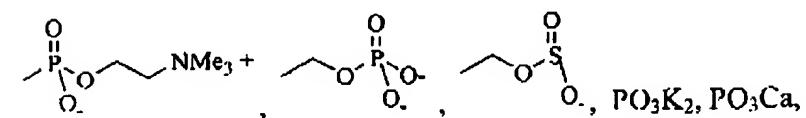
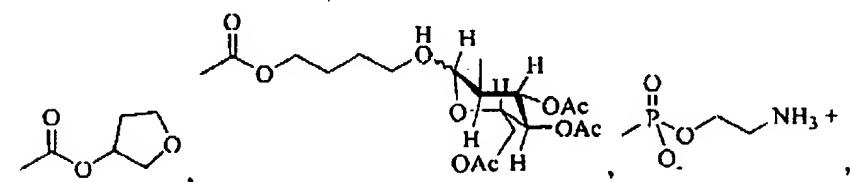
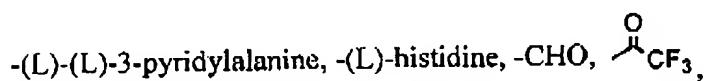
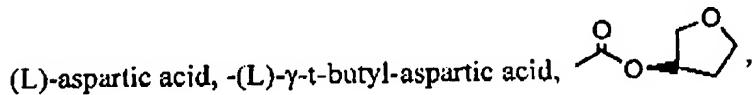
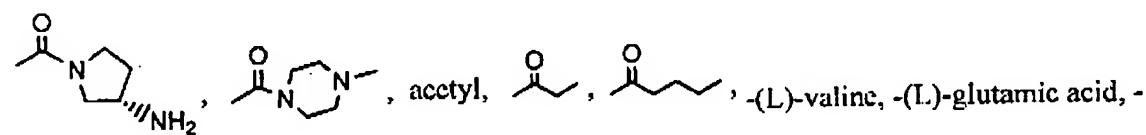
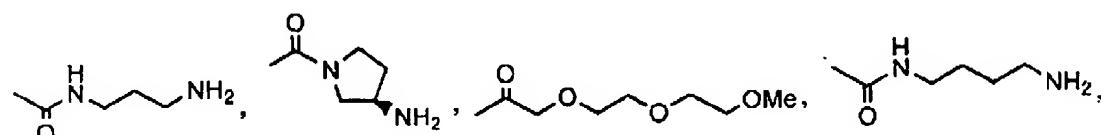
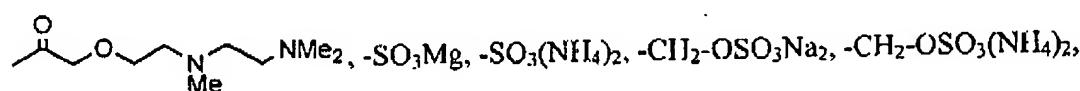
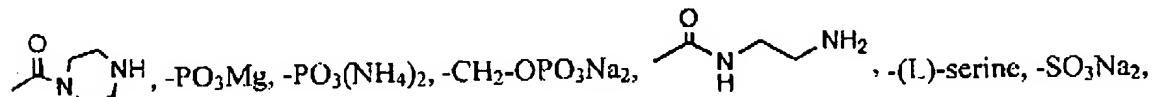
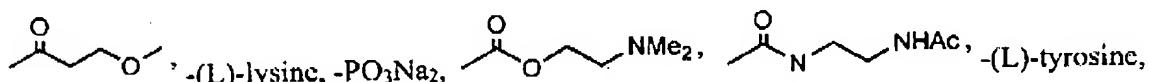
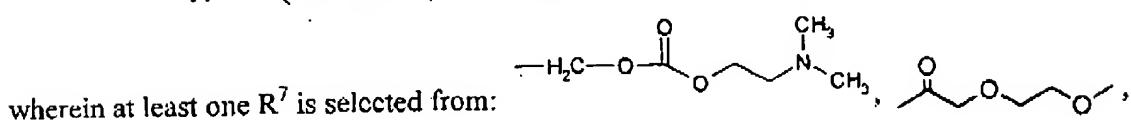
$-N(R^3)-S(O)_n(R^3)$, $-N(R^3)-S(O)_n-N(R^3)_2$, $-S-NR^3-C(O)R^3$, $-C(S)N(R^3)_2$, $-C(S)R^3$, $-NR^3-C(O)OR^3$, $-O-C(O)OR^3$, $-O-C(O)N(R^3)_2$, $-NR^3-C(S)R^3$, $=N-OH$, $=N-OR^3$, $=N-N(R^3)_2$, $=NR^3$, $=NNR^3C(O)N(R^3)_2$, $=NNR^3C(O)OR^3$, $=NNR^3S(O)_n-N(R^3)_2$, $-NR^3-C(S)OR^3$, $-NR^3-C(S)N(R^3)_2$, $-NR^3-C[=N(R^3)]-N(R^3)_2$, $-N(R^3)-C[=N-NO_2]-N(R^3)_2$, $-N(R^3)-C[=N-NO_2]-OR^3$, $-N(R^3)-C[=N-CN]-OR^3$, $-N(R^3)-C[=N-CN]-N(R^3)_2$, $-OC(O)R^3$, $-OC(S)R^3$, $-OC(O)N(R^3)_2$, $-C(O)N(R^3)-N(R^3)_2$, $-O-C(O)N(R^3)-N(R^3)_2$, $O-C(O)N(OR^3)(R^3)$, $N(R^3)-N(R^3)C(O)R^3$, $N(R^3)-OC(O)R^3$, $N(R^3)-OC(O)R^3$, $N(R^3)-OC(O)R^3$, $N(R^3)-OC(S)N(R^3)_2$, $-OC(S)N(R^3)(R^3)$, or PO_3-R^3 ; C_2-C_{15} alkynyl which contains one or more substituents selected from oxo, $[[halo,]]$ $-CF_3$, $-OCF_3$, $-NO_2$, azido, $-SH$, $[-SR^3,]$ $-N(R^3)-N(R^3)_2$, $-O-N(R^3)_2$, $-(R^3)N-O-(R^3)$, $[-N(R^3)_2,]$ $-CO_2R^3$, $-C(O)-N(R^3)_2$, $-S(O)_n-N(R^3)_2$, $-N(R^3)-C(O)-R^3$, $-N(R^3)-C(O)-N(R^3)_2$, $-N(R^3)-C(O)-S(R^3)$, $-C(O)-R^3$, $[-S(O)_n-R^3,]$ $-N(R^3)-S(O)_n(R^3)$, $-N(R^3)-S(O)_n-N(R^3)_2$, $-S-NR^3-C(O)R^3$, $-C(S)N(R^3)_2$, $-C(S)R^3$, $-NR^3-C(O)OR^3$, $-O-C(O)OR^3$, $-O-C(O)N(R^3)_2$, $-NR^3-C(S)R^3$, $=N-OII$, $=N-OR^3$, $=N-N(R^3)_2$, $=NR^3$, $=NNR^3C(O)N(R^3)_2$, $=NNR^3C(O)OR^3$, $=NNR^3S(O)_n-N(R^3)_2$, $-NR^3-C(S)OR^3$, $-NR^3-C(S)N(R^3)_2$, $-NR^3-C[=N(R^3)]-N(R^3)_2$, $-N(R^3)-C[=N-NO_2]-N(R^3)_2$, $-N(R^3)-C[=N-NO_2]-OR^3$, $-N(R^3)-C[=N-CN]-OR^3$, $-N(R^3)-C[=N-CN]-N(R^3)_2$, $-OC(O)R^3$, $-OC(S)R^3$, $-OC(O)N(R^3)_2$, $-C(O)N(R^3)-N(R^3)_2$, $-O-C(O)N(R^3)-N(R^3)_2$, $O-C(O)N(OR^3)(R^3)$, $N(R^3)-N(R^3)C(O)R^3$, $N(R^3)-OC(O)R^3$, $N(R^3)-OC(O)R^3$, $N(R^3)-OC(O)R^3$, $N(R^3)-OC(S)N(R^3)_2$, $-OC(S)N(R^3)(R^3)$, or PO_3-R^3 ; with the proviso that when R^7 is H, E' is SO_2 , G is H or alkyl, and when B is present or when B is not present and R^4 is $C(O)$, D' may not be C, C_{15} alkyl substituted with one substituent selected from $N(R^3)_2$ or $S(O)_n-R^3$, or substituted with two $N(R^3)_2$ substituents.

7. (Currently amended) The compound according to claim 5 wherein:

D' is selected from C_1-C_{15} alkyl or C_2-C_{15} alkenyl, each of which contains one or more substituents selected from $-SH$, $[-SR^3,]$ $-CO_2R^3$, $-C(O)-N(R^3)_2$, $-S(O)_n-N(R^3)_2$ or $-N(R^3)-C(O)-R^3$; with the proviso that when R^7 is H, E' is SO_2 , G is H or alkyl, and when B is present or when B is not present and R^4 is $C(O)$, D' may not be C_1-C_{15} alkyl substituted with one substituent selected from SR^3 .

8. (Canceled)

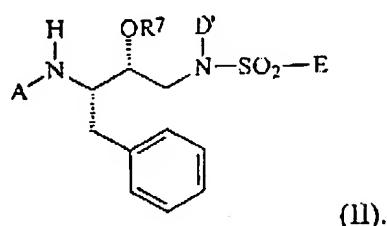
9. (Withdrawn) The compound according to any one of claims 1 to 7,



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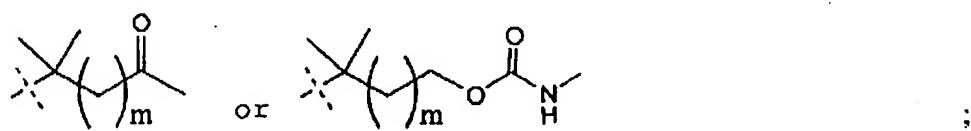
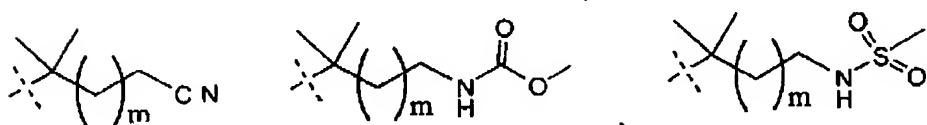
PO_3 -spermine, PO_3 -(spermidine)₂ or PO_3 -(meglamine)₂.

10. (Currently amended) The compound according to claim [[8]] 1, having the formula II:



11. (Cancelled)

12. (Original) The compound according to claim 10, wherein:
 D' is $-\text{CH}_2\text{-R}''$; and
 R'' is selected from

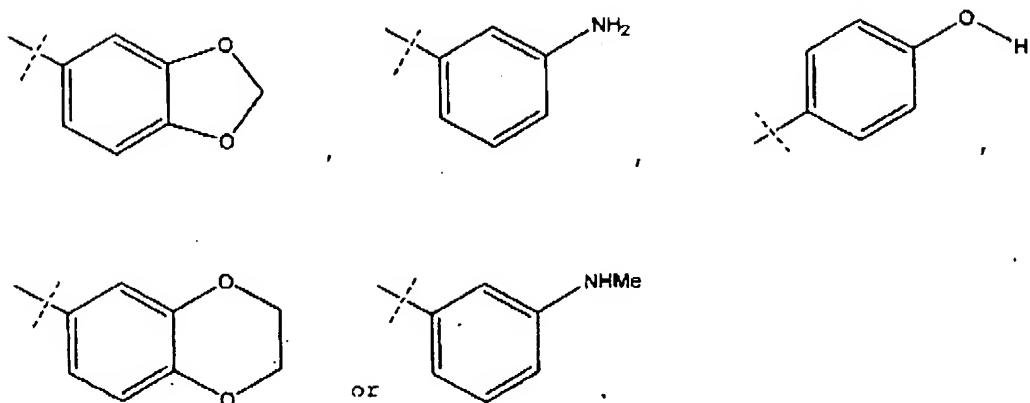


wherein m is 0 to 3.

13. (Original) The compound according to claim 10, wherein E is selected from

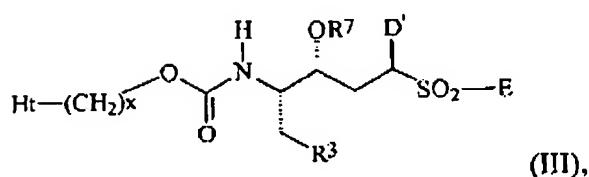
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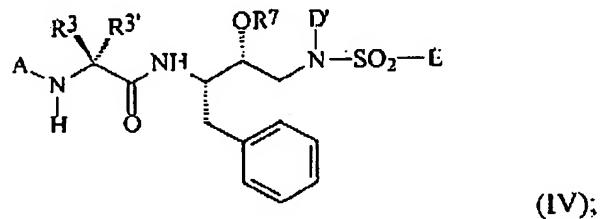
14. (Withdrawn) The compound according to claim 10, wherein R⁷ is -PO₃²⁻

15. (Previously presented) The compound according to claim 1, having the formula III:



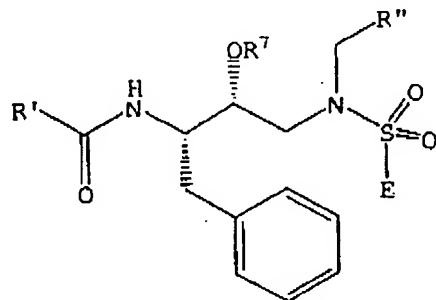
wherein x = 1.

16. (Withdrawn) The compound according to claim 1, having the formula IV:



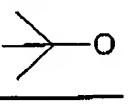
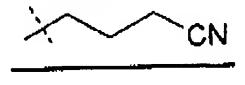
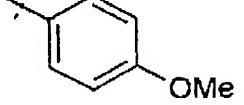
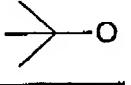
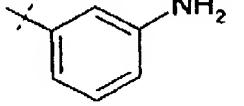
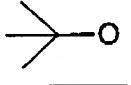
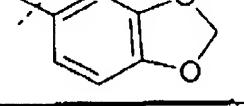
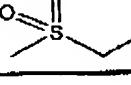
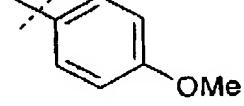
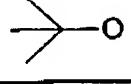
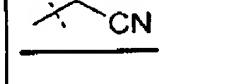
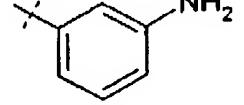
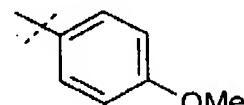
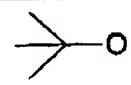
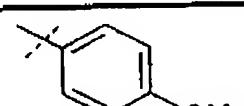
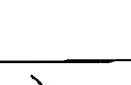
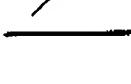
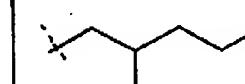
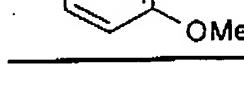
wherein R³ is selected from H, Ht, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₃-C₆ cycloalkyl or C₅-C₆ cycloalkenyl; wherein any member of said R³, except H, is optionally substituted with one or more substituents selected from -OR², -C(O)-NH-R², -S(O)_n-N(R²)(R²), -N(R²)₂, -N(R²)-C(O)-O(R²), -N(R²)-C(O)-N(R²), -N(R²)-C(O)-(R²), -N(R²-OR²)₂, -C(O)-Ht, Ht, -CN, -SR², -CO₂R², or NR²-C(O)-R².

17. (Currently amended) The compound according to claim 1, wherein said compound is selected from any one of compound numbers: 1, 2, 3, 4, 5, 6, 22, 127, 203, 234, 277, 278, 279, 363, and 364;



wherein R⁷ is H; and

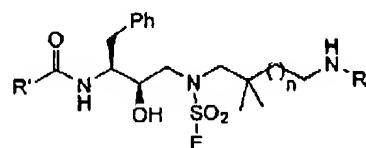
Compound	R'	R''	E
1			
2			
3			

Compound	R'	R''	E
<u>4</u>			
<u>5</u>			
<u>6</u>			
<u>22</u>			
<u>127</u>			
<u>203</u>			
<u>234</u>			
<u>277</u>			
<u>278</u>			

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13

Compound	R'	R''	E
279			



Compound	R'	E	n	R
363			3	
364			3	

18-22. (Canceled)

23. (Currently amended) A composition comprising a compound according to any one of claims 1-10 and 12-17 1-7, 10, 12, 13, 15, and 17 or a pharmaceutically acceptable salt thereof in a therapeutically effective amount an amount sufficient to detectably inhibit aspartyl protease activity in a patient, and a pharmaceutically acceptable carrier.

24. (Original) The composition according to claim 23, further comprising an additional antiviral agent other than a compound of formula (I).

25. (Original) The composition according to claim 23, wherein said composition is formulated as a pharmaceutically acceptable, orally available tablet or capsule.

26. (Currently amended) A method of treating an HIV virus infection in a human comprising the step of administering to said human a composition according to any one of claims 23 to 25 claim 23.

27. (Currently amended) The method according to claim 26, further comprising the step of

administering to said patient an additional antiviral agent other than a compound of formula I, wherein said additional antiviral agent is administered prior to, simultaneously with or following administration of said composition.

28. (New) A method of treating an HIV virus infection in a human comprising the step of administering to said human a composition according to claim 24.

29. (New) The method according to claim 28, further comprising the step of administering to said patient a second additional antiviral agent other than a compound of formula I, wherein said second additional antiviral agent is administered prior to, simultaneously with or following administration of said composition.

30. (New) A method of treating an HIV virus infection in a human comprising the step of administering to said human a composition according to claim 25.

31. (New) The method according to claim 30, further comprising the step of administering to said patient an additional antiviral agent other than a compound of formula I, wherein said additional antiviral agent is administered prior to, simultaneously with or following administration of said composition.